



Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US

Sheet 2 of 25

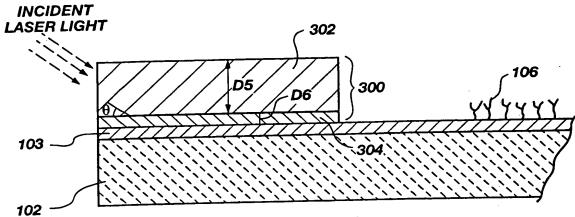


Fig. 3A

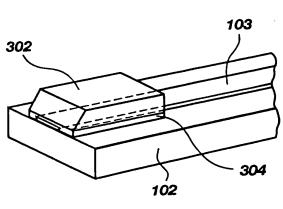


Fig. 3B

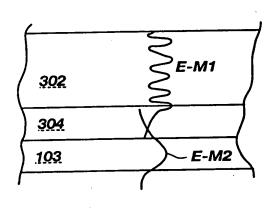


Fig. 3C

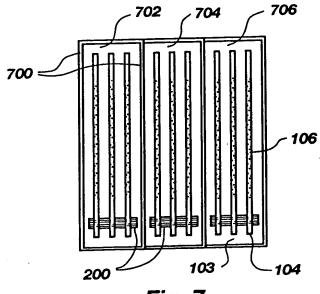
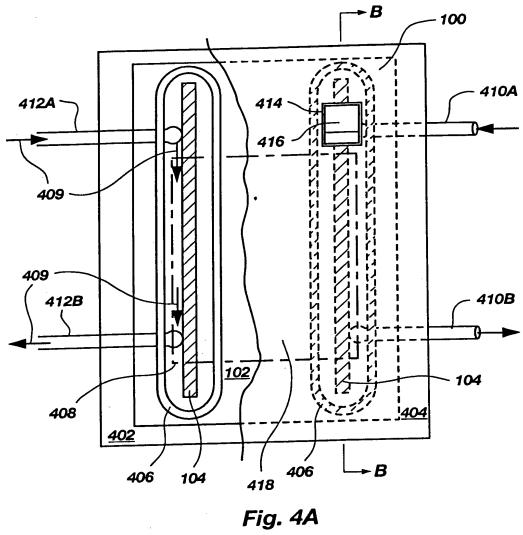


Fig. 7



Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 3 of 25



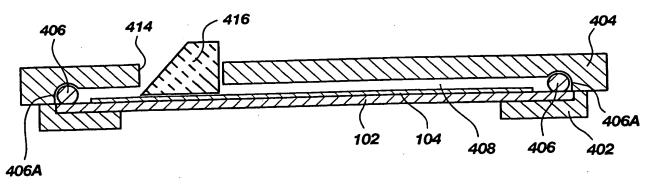
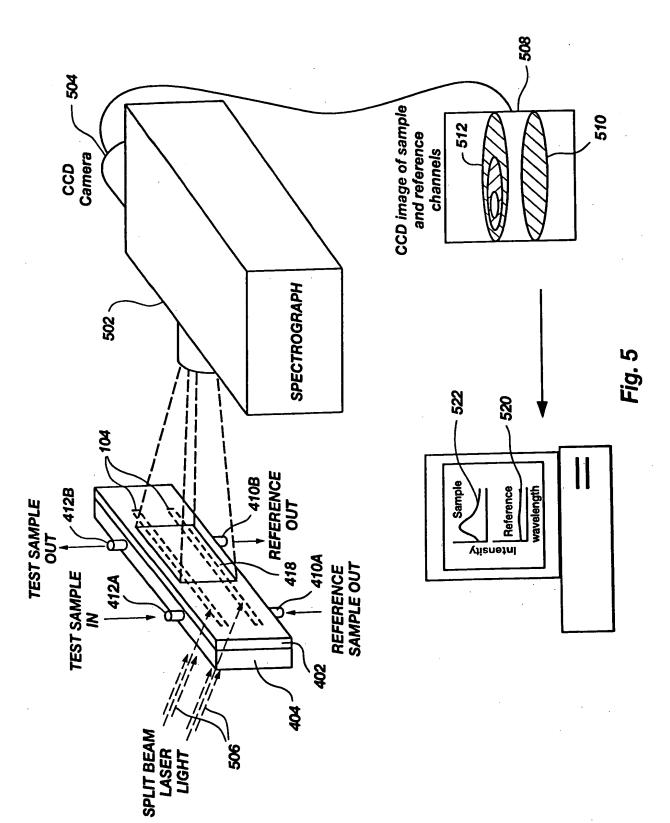


Fig. 4B



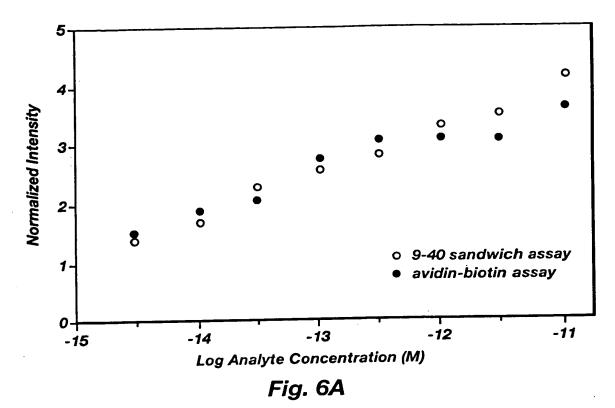
Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US

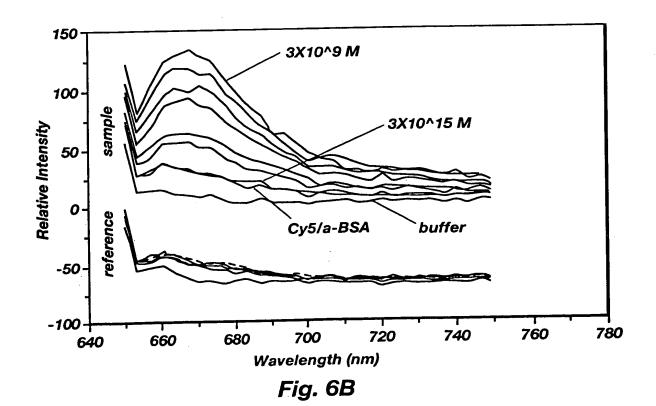
Sheet 4 of 25





TITLE: COMPOSITE WAVEGUIDE FOR SOLID PHASE BINDING ASSAYS
Inventor: Reichert et al.
Serial No.: 09/185,318
Docket No.: 0274.02-2978.1US
Sheet 5 of 25





DEC 1 3 2004

TITLE: COMPOSITE WAVEGUIDE FOR SOLID PHASE BINDING ASSAYS Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 6 of 25

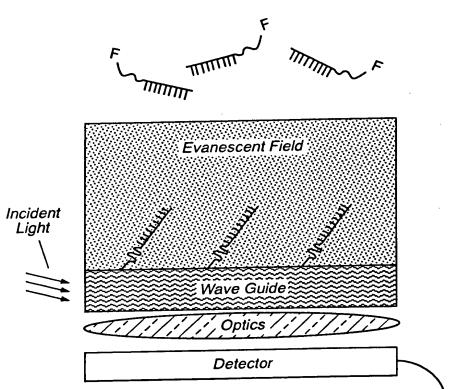


Fig. 8

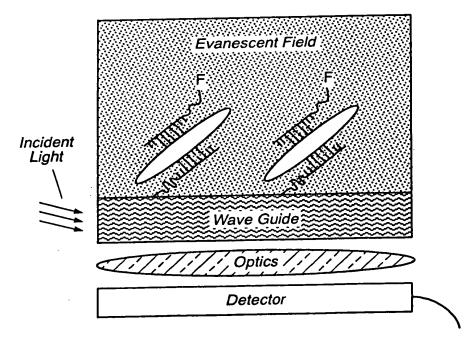


Fig. 9

DEC 1 3 2004

TITLE: COMPOSITE WAVEGUIDE FOR SOLID PHASE BINDING ASSAYS Inventor: Reichert et al.

Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 7 of 25



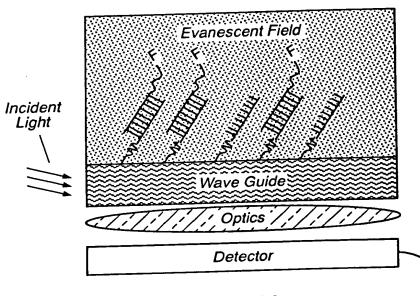


Fig. 10

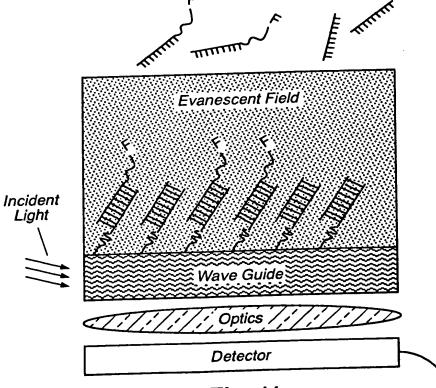
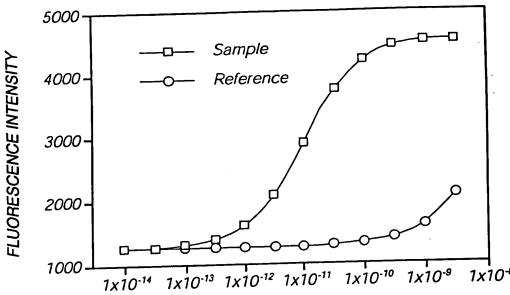


Fig. 11

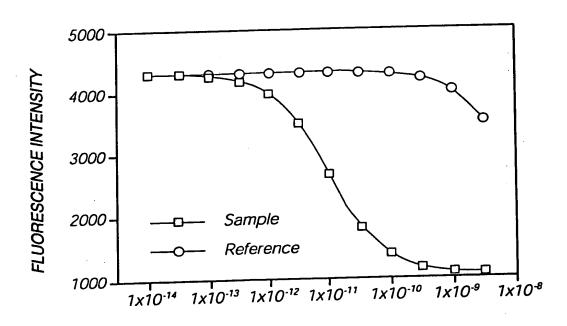


Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 8 of 25



OLIGONUCLEOTIDE CONCENTRATION (MOLAR)

Fig. 12



OLIGONUCLEOTIDE CONCENTRATION (MOLAR)

Fig. 13



Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US

Sheet 9 of 25

WITH SURFACE BOUND ANTICOMPLIMENT ON POLYSTYRENE WAVEGUIDE EQUILIBRIUM BINDING ISOTHERM OF CYS-LABLED OLIGONUCLEOTIDE (CURVE FIT SHOWN)

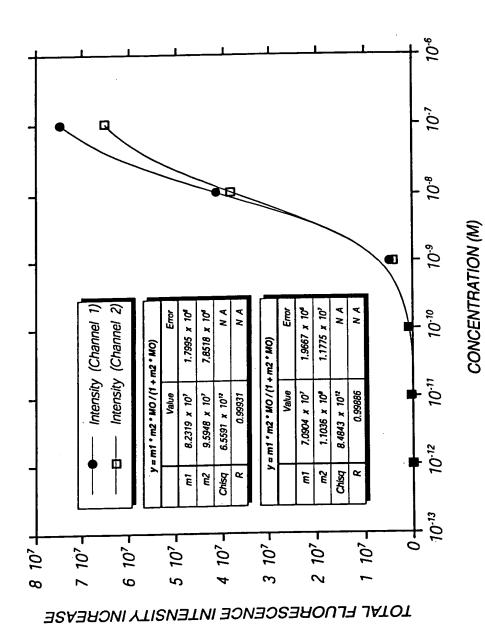


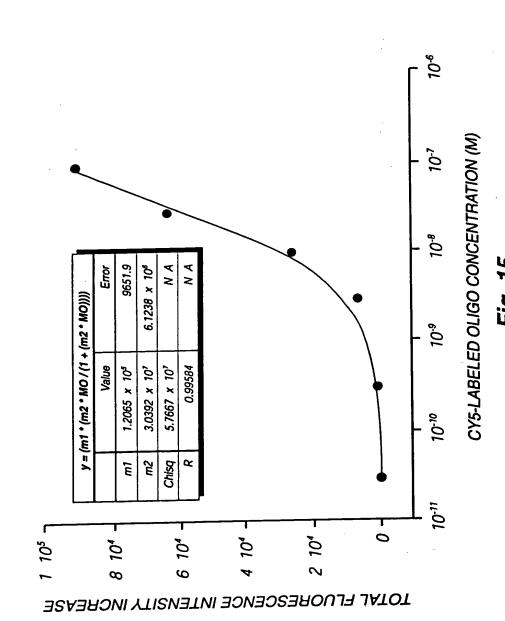
Fig. 14





TITLE: COMPOSITE WAVEGUIDE FOR SOLID PHASE BINDING ASSAYS Inventor: Reichert et al. Serial No.: 09/185,318
Docket No.: 0274.02-2978.1US Sheet 10 of 25

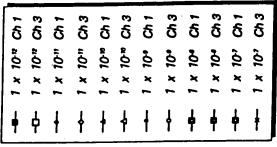
WITH SURFACE BOUND ANTICOMPLIMENT ON INTIGRATED OPTIC WAVEGUIDE EQUILIBRIUM BINDING ISOTHERM OF CYS-LABLED OLIGONUCLEOTIDE (CURVE FIT SHOWN)

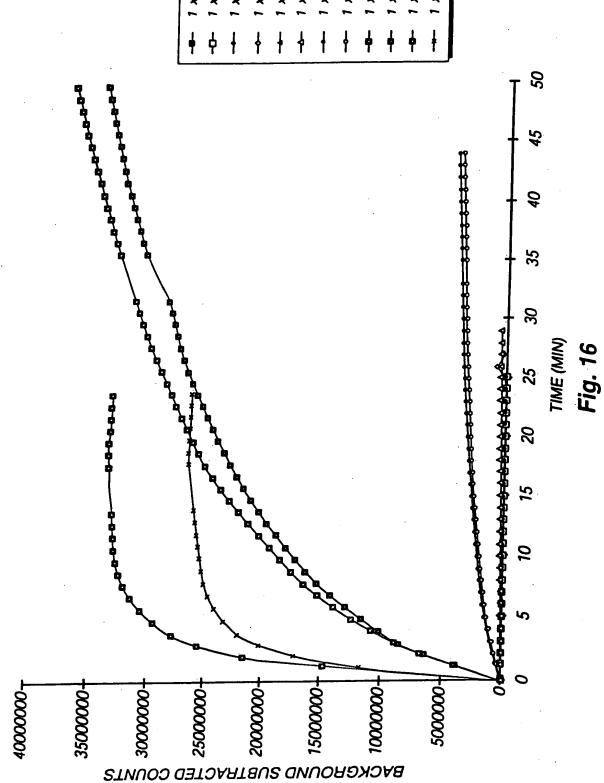


KINETICS OF INCREASING OLIGO TRACER CONCENTRATION (ON ONE POLYSTYRENE WG)

TITLE: COMPOSITE WAVEGUIDE FOR SOLID PHASE BINDING ASSAYS

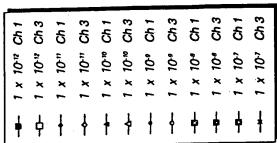
Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 11 of 25

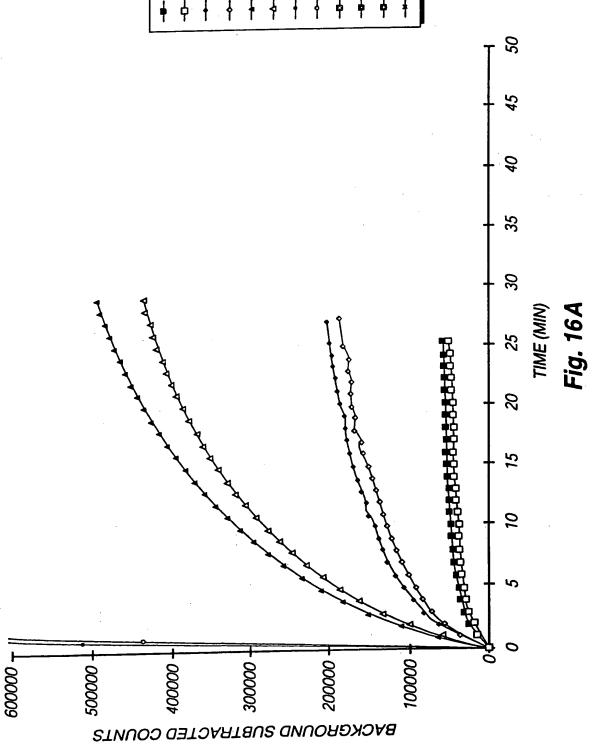




KINETICS OF INCREASING OLIGO TRACER CONCENTRATION (ON ONE WG)

Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 12 of 25







Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 13 of 25

	В	С	D	Е	F	G	Н
1		1x10 ⁻¹² M					
2							
3		Raw Fluc	rescence Kir	netic Data	Background	Subtracted	
4	Time (min)	Ch1		Ch3	1x10 ⁻¹² Ch1		1x10 ⁻¹² Ch3
5	0	1031980		947053	0		0
6	1	1051720		964657	19740		17604
7	2	1059810		971060	27830		24007
8	3	1064300		975759	32320		28706
9	4	1066790		977556	34810		30503
10	5	1070240		979930	38260		32877
11	6	1073240		985923	41260		38870
12	7	1077290		982526	45310		35473
13	8	1077920		986607	45940		39554
14	9	1079540		984734	47560		37681
15	10	1080120		988538	48140		41485
16	11	1083400		988133	51420		41080
17	12	1081750		988906	49770		41853
18	13	1083850		990135	51870		43082
19	14	1084520		993928	52540		46875
20	15	1086060		991629	54080		44576
21	16	1087080		993243	55100		46190
22	17	1085270		994081	53290		47028
23	18	1086270		992415	54290		45362
24	19	1087740		993538	55760		46485
25	20	1087370		995980	55390		48927
26	21	1087260		994168	55280		47115
27	22	1087940		995014	55960		47961
28	23	1089060		996124	57080		49071
29	24	1088160		995082	56180		48029
30	25	1089260		997941	57280		50888

Fig. 17

DEC 1 3 2004

TITLE: COMPOSITE WAVEGUIDE FOR SOLID PHASE BINDING ASSAYS

Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 14 of 25

-	К	L	M	N	0	Р	Q
1		1x10 ⁻¹¹ M					
2		_ 12.1					
3		Raw Fluo	rescence Ki	netic Data	Background Subtracted Kinetic Data		
4	Time (min)	Ch1		Ch3	1x10 ⁻¹¹ Ch1		1x10 ⁻¹¹ Ch3
5	0	1.112100		1013190	0		0
6	1	1152800		1051900	40700		38710
7	2	1177670		1071660	65570		58470
8	3	1195110		1086710	83010		73520
9	4	1206770		1098220	94670		85030
10	5	1218050		1107530	105950		94340
11	6	1226500		1115620	114400		102430
12	7	1235640		1122820	123540		109630
13	8	1242310		1131140	130210		117950
14	9	1250250		1135680	138150		122490
15	10	1253080		1140810	140980		127620
16	11	1262270		1146620	150170		133430
17	12	1264930		1151130	152830		137940
18	13	1271750		1155150	159650		141960
19	14	1275570		1160520	163470		147330
20	15	1279790		1162120	167690		148930
21	16	1283360		1170450	171260		157260
22	17	1289100		1172750	177000	<u></u>	159560
23	18	1292270		1180160	180170		166970
24	19	1292130		1180470	180030	<u> </u>	167280
25	20	1296600		1182910	184500		169720
26	21	1300090		1185730	187990		172540
27	22	1302750		1186670	190650		173480
28	23	1304940		1189090	192840	ļ <u> </u>	175900
29	24	1308560		1188140	196460		174950
30	25	1309440		1195230	197340		182040
31	26	2002360		1980930	890260		967740
32	27	1314400		1198680	202300		185490



Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 15 of 25

	Т	U	V	W	Х	Υ	Z
1		1x10 ⁻¹⁰ M					
2							
3		Raw Fluo	rescence Ki	netic Data	Background	Subtracted	Kinetic Data
4	Time (min)	Ch1		Ch3	1x10 ⁻¹⁰ Ch1		1x10 ⁻¹⁰ Ch3
5	0	1432650		1312580	0		0
6	1	1500170		1373250	67520		60670
7	2	1542830		1411670	110180		99090
8	3	1582310		1444560	149660		131980
9	4	1614050		1476000	181400		163420
10	5	1641770		1498500	209120		185960
11	6	1666940		1520160	234290		207580
12	7	1691120		1541210	258470		228630
13	8	1700740		1560130	278090		247550
14	9	1730010		1575870	297360		263290
15	10	1747540		1599050	314890		276470
1.6	11	1763960		1605980	331310		293400
17	12	1777990		1620430	345340		307850
18	13	1789310		1630300	356660		317720
19	14	1804540		1639820	371890		327240
20	15	1816140		1655440	383490		342860
21	16	1827680		1663840	395033		351260
22	17	1840680		1674570	408030		361990
23	18	1851760		1680090	419110		367510
24	19	1858720		1693450	426070		380870
25	20	1869390		1699100	436740		386520
26	21	1877230		1708640	444580		396060
27	22	1884240		1714860	451590		402280
28	23	1891760		1720530	459110		407950
29	24	1899320		1725140	466670		412560
30	25	1904700		1733780	472050		421200
31	26	1910260		1739570	477610		426990
32	27	1917760		1741990	485110		429410
33	28	1924070		1750590	491420		438010
34	29	1926800		1751600	494150		439020

Fig. 19



Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 16 of 25

	AC	AD	AE	AF	AG	AH .	Al
1	 	1x10 ⁻⁹ M					ļ
2	 					·	<u> </u>
3		Raw Fluor	rescence Kir	netic Data		Subtracted k	
4	Time (min)	Ch1		Ch3	1x10 [®] Ch1		1x10 ^e Ch3
5	0	2277600		2066020	0		0
6	1 1	2791580		2504350	513980		438330
7	2	3116840		2792860	839240		726840
8	3	3377790		3021480	1100190		955460
9	4	3593810		3217180	1316210		1151160
10	5	3782480		3389790	1504880		1323770
11	6	3954890		3544790	1677290		1478770
12	1 7	4107890		3684630	1830290		1618610
13	8	4254390		3819870	1976790		1753850
14	9	4384410		3940160	2106810		1874140
15	10	4503520		4046970	2225920		1980950
16	11	4617170		4155710	2339570		<i>2089690</i>
17	12	4720460		4250340	2442860		2184320
18	13	4825950		4345730	2548350		2279710
19	14	4916650		4431590	2639050		2365570
20	15	5012020		4517220	2734420		2451200
21	16	5101450		4600800	2823850		2534780
22	17	5184010		4676650	2906410		2610630
23	18	5258160		4747450	2980560		2681430
24	19	5331160		4812870	3053560		2746850
25	20	5403100		4876800	3125500		2810780
26	21	5469290		4940820	3191690		2874800
27	22	5527850		4999840	3250250		2933820
28	23	5590790		5054350	3313190		<i>2988510</i>
29	24	5645270		5109750	3367670		3043730
30	25	5700390		5159770	3422790		3093750
31		5752500		5207200	3474900		3141180
32	l	5799990		5254210	3522390	· · · · · · · · · · · · · · · · · · ·	3188190
33		5849310		5295550	3571710		3229530
34		5894420		5337760	3616820		3271740
35		5931460		5374030	<i>3653860</i>		3308010
36		5973550		5412550	3695950		3346530
37		6010260		5451210	3732660		3385190
38		6044600		5482710	3767000		3416690
39		0		0			
40		6116470		<i>5550920</i>	<i>3838870</i>		3484900
41		6147630		5578310	3870030		3512290
42		6174870		5608720	3897270		3542700
43		6204650		5636190	3927050		3570170
44		6231100		5654760	3953500		3588740
45		6250750		5682210	3973150		3616190
46		6271150		5699130	3993550		3633110
47	 	6293540		5723860	4015940		3657840
48	 	6307640		5731930	4030040		3665910
49		6330810		5752080	4053210		3686060



Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US

Sheet 17 of 25

1	AL	AD	AN	AF	AG	AQ	Al
50	<u> </u>	21973900		23388700	35244420		32889720
		22108900		20474300	35514420		33060920
51 52		22225000	·····	20568500	35746620		33249320
		22324000		20659300	35944620		33430920
53		22442200	_ 	20773700	36181020		33659720
54 55		22524700		20894600	36346020		33901520

Fig. 21



Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 18 of 25

			ANI	T AO I	AP	AQ	AR
	AL	AM	AN	 			
1		1x10 ⁻⁸ M					
2		Davi Flue	rescence Ki	netic Data	Background	Subtracted K	inetic Data
3			rescence N	Ch3	1x10 ⁻⁶ Ch1		1x10 [®] Ch3
4	Time (min)	Ch1		7887680	0		0_
5	0	8703380		11737900	3999320		3850220
6	1	12702700		14403300	6717220		6515620
7	2	15420600		16383800	8950020		8496120
8	3	17653400		17999500	10861720		10111820
9	4	19565100 21173800		19524900	12470420		11637220
10	5	22610500		20827400	13907120		12939720
11	6	23890100		22128500	15186720		14240820
12	7	25099600		23241100	16396220		15353420
13	8	26178400		24236400	17475020		16348720
14	9	27228700		25135700	18525320		17248020
15	10	28247800		26050500	19544420		18162820
16	11 12	29125600		26871000	20422220		18983320
17	13	29933500		27640300	21230120		19752622
18	14	30841700		28312900	22138320		20425220
<u>19</u>	15	31585800		29031300	22882420		21143620
20	16	32377400		29684100	23674020		21796420
21	17	33057900		30278200	24354520		22390520
22	18	33764700		30843200	25061320		22955520
23	19	34358100		31395300	25654720		23507620
<u>24</u> 25	20	34882300		31916400	26178920		24028720
26	21	35476100		32442900	26772720		24555220 25071720
27	22	36033800		32959400	27330420		25566020
28	23	36568900		33453700	27865520		26012820
29	24	37028500		33900500	28325120		26370720
30	25	37445200		34258400	28741820		26745920
31		37891100		34633600	29187720		27141820
32		38356200		35029500	29652820		27393220
33		38764900		35280900	30061520	 	27680320
34		39118800		35568000	30415420		28028520
35		39418600		35916200	30715220 31111620		28299520
36		39815000		36187200	31437520		28554320
37		40140900		36442000	3143/320		1 2000
38		0		0			
39		0		0			
40		0		10169700	32717020		30449720
41		20710200		19168700 19328900	33030020		30770120
42		20866700			33325820		31099120
43		21014600		19483400	33633020		31361120
44		21168200		19624400 19780300	33914620		31672920
45		21309000			34212420		31920520
46		21457900		19904100 20019800	34540220		32151920
47		21621800		20140200	34779820		32392720
48		21741600		20140200	35010220		32608720
49		21856800		1 20240200	300.0220	<u> </u>	

Fig. 22



Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 19 of 25

Δ1	T AM T	AN	AO	AP	AQ	AR
			23388700	35244420		32889720
			20474300	35514420		33060920
			20568500	35746620		33249320
			20659300	35944620		33430920
			20773700	36181020		33659720
			20894600	36346020		33901520
	AL	AL AM 21973900 22108900 22225000 22324000 22442200 22524700	21973900 22108900 22225000 22324000 22442200	21973900 23388700 22108900 20474300 22225000 20568500 22324000 20659300 22442200 20773700	21973900 23388700 35244420 22108900 20474300 35514420 22225000 20568500 35746620 22324000 20659300 35944620 22442200 20773700 36181020	AL AM AM 35244420 21973900 23388700 35244420 22108900 20474300 35514420 22225000 20568500 35746620 22324000 20659300 35944620 22442200 20773700 36181020

Fig. 23



TITLE: COMPOSITE WAVEGUIDE FOR SOLID PHASE BINDING ASSAYS Inventor: Reichert et al. Serial No.: 09/185,318

Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 20 of 25

	AU	AV	AW	AX	AY	AZ	ВА
	AU	1x10 ⁻⁷ M					
1		IXIO IVI					
2		Baw Fluo	rescence K	inetic Data	Background Subtracted Kinetic Data		
3	Time (min)	Ch1		Ch3	1x10 ⁻⁷ Ch1		1x10 ⁻⁷ Ch3
4	0	28245300		26212000	0		0
5	1	35584600		32050700	14678600		11677400
6	2	39026200		34787600	21561800		17151200
7	3	41044300		36276700	25598000		20129400
8	4	42114200		37171300	27737800		21918600
9	5	42966200		37774800	29501800		23125600
10	6	43538500		38208800	30586400		23993600
11	7	43931600		38462300	31372600		24500600
12	8	44268000		38663800	32045400		24903600
13	9	44452200		38797700	32413800		25171400
14	10	44584500		38940900	32678400		25457800
15	11	44707800		39005700	32925000		25587400
16	12	44741300		39075000	32992000		25726000
17	13	44762600		39158200	33034600		25892400
18 19	14	44825600		39210600	33160600		25997200
20	15	0		0		<u> </u>	
21	16	0		0.			
<u> </u>	17	0		0			
22	18	22483000		19739100	33441400		26532400
24	19	22486100		19752000	33453800		26584000
25	20	22481800		19759100	33436600		26612400
26	21	22462900		19742500	33361000		26546000
27	22	22437500		19722500	33259400		26466000
28	23	22445100		19723700	33289800		26470800
29	24	22415700		19714400	33172200		26433600

Fig. 24



Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 21 of 25

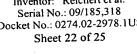
Total Increase in	Fluorescence (E	quilibrium) Dat a		
Concentration (M)	Channel 1 counts	Channel 3 counts	Total counts Ch1	Total counts Ch3
$\frac{1 \times 10^{-12}}{1}$		<i>50888</i>	57280	50888
$\frac{1 \times 10^{-11}}{1 \times 10^{-11}}$		185490	<i>259580</i>	236378
1 x 10 ⁻¹⁰		439020	753730	675398
$\frac{1 \times 10^{-9}}{1 \times 10^{-9}}$		3686060	4806940	4361458
$\frac{1 \times 10^{-8}}{1 \times 10^{-8}}$		33901520	41152960	38262978
$\frac{1 \times 10^{-7}}{1 \times 10^{-7}}$		26433600	74325160	64696578

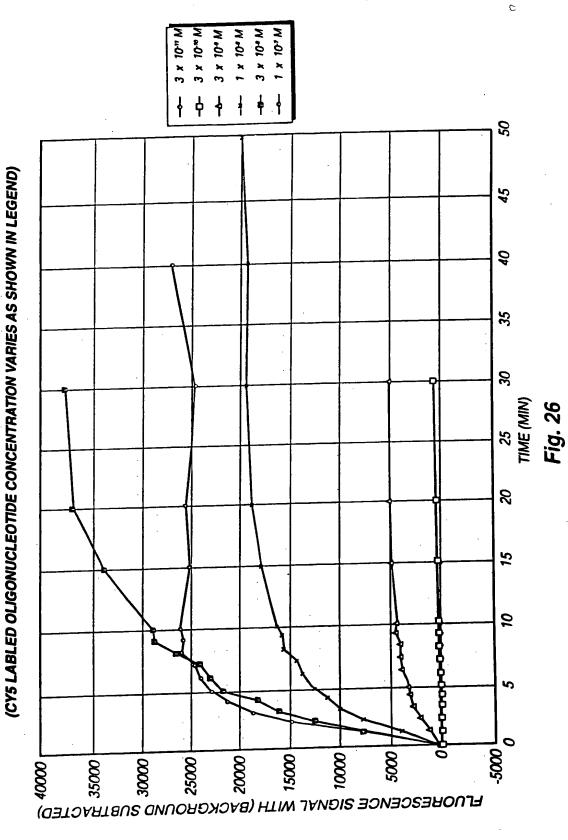
Fig. 25

BINDING KINETICS CURVES OF CYS-LABLED OLIGONUCLEOTIDE SOLUTIONS ON A SION INTEGRATED OPTIC WAVEGUIDE

TITLE: COMPOSITE WAVEGUIDE FOR SOLID PHASE BINDING ASSAYS

Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US







Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 23 of 25

IO OLIGO ASSAY

	С	D	E	F	G	Н	1
5			rescence Kir	netic Data			
6							
7		Concer	ntration				7.2
8	Time (min)	3 x 10 ⁻¹¹ M	3 x 10 ⁻¹⁰ M	3 x 10 ⁻⁹ M	1 x 10 ⁻⁸ M	3 x 10 ⁻⁸ M	1 x 10 ⁻⁷ M
9	0	13403	13921	16827	32542	77025	174425
10	1	13441	13915	18007	36606	84937	182107
11	2	13458	14058	18909	40339	89541	189164
12	3	13469	14019	19556	42439	93142	193135
13	4	13547	14145	19982	43697	95188	195511
14	5	13454	14115	20268	45324	98929	197588
15	6	13538	14187	20730	46146	100143	198491
16	7	13467	14192	20882	46895	101259	198996
17	8	13489	14211	20965	48048	103359	200235
18	9	13431	14256	21357	48227	105623	200147
19	10	13485	14176	21233	48766	105865	200469
20	15	13455	14262	21763	50251	110981	199558
21	20		14379	21921	51306	113911	199813
22	30		14377	21867	51825	114547	198883
23	40				51559		201156
24	50				51908		
25	60						<u> </u>

Fig. 27



TITLE: COMPOSITE WAVEGUIDE FOR SOLID PHASE BINDING ASSAYS Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US

Sheet 24 of 25

IO OLIGO ASSAY

	С	J	К	L	М	N	0
5			Background Subtracted F		Kinetic Data		· · · · · · · · · · · · · · · · · · ·
6							
7		Conce	ntration				7
8	Time (min)	3 x 10 ⁻¹¹ M	3 x 10 ⁻¹⁰ M	3 x 10 ⁻⁹ M	1 x 10 ⁻⁸ M	3 x 10 ⁻⁸ M	1 x 10 ⁻⁷ M
9	0	. 0	0	0	0	0	0
10	1	38	-6	1180	4064	7912	7682
11	2	55	137	2082	7797	12516	14739
12	3	66	98	2729	9897	16117	18710
13	4	144	224	3155	11155	18163	21086
14	5	51	194	3441	12782	21904	23163
15	6	135	266	3903	13604	23118	24066
16	7	64	271	4055	14353	24234	24571
17	8	86	290	. 4138	15506	26370	25810
18	9	28	355	4530	15685	28598	25722
19	10	82	255	4406	16224	28404	26044
20	15	52	341	4936	17709	33956	25133
21	20		458	5094	18764	36886	25388
22	30		456	5049	19283	37522	24458
23	40				19017		26731
24	50				19366		
25	60						

Fig. 28



Inventor: Reichert et al. Serial No.: 09/185,318 Docket No.: 0274.02-2978.1US Sheet 25 of 25

IO OLIGO ASSAY

<u> </u>	Q	R	S	T	U
5					
6	Total Increase in	n Fluorescence (E	quilibrium) Data		
7				Total accumic	
8		Concentration	Counts	Total counts	
9		3 x 10 ⁻¹¹	52	52	
10		3 x 10 ⁻¹⁰	456	508	
11		0.000000003	5049	5557	
12		0.00000001	19366	24923	
13		0.00000003	37522	62445	
14		0.0000001	26731	89176	
15					
16					
17					

Fig. 29